INFORMATION SHEET AND INFORMED CONSENT FORM FOR PATIENT PARTICIPATION IN A CLINICAL TRIAL

Official trial title

Exploring cognitive recovery: the impact of sensor-based upper-limb robotic rehabilitation in neurological and neurodegenerative disorders

Official trial title in more patient-friendly terms

In this study, we aim to understand how an upper-limb rehabilitation treatment can influence cognitive functions, such as memory and attention. We want to understand whether, and how, improving motor abilities may have a positive impact on the way we think and behave.

Setting/context where the trial will be conducted

IRCCS Centro Neurolesi Bonino Pulejo

Coordinating center (if different from the site where the trial takes place) and trial coordinator

Coordinating center:
_____
Trial coordinator: Dr. Desirèe Latella _____

Registry in which the trial has been or will be registered (if applicable) and any available identification code

Identification code: CROSS-ND
Registry:
_____

Principal Investigator

Name: Desirèe Latella _____
Affiliation: IRCCS Centro Neurolesi Bonino Pulejo _____

Sponsor/Funding organization

Ethics Committee

Local Ethics Committee – IRCCS Centro Neurolesi "Bonino-Pulejo"

This document is composed of the following sections:

A. PREMISE
B. INFORMATION SECTION. TRIAL SUMMARY: KEY INFORMATION
C. INFORMATION SECTION. ADDITIONAL DETAILS
D. CONSENT EXPRESSION SECTION
ATTACHMENTS
ADDITIONAL DOCUMENTS

Dear Madam/Sir, the information contained in the following information sheet is very detailed. We ask you to agree to participate in the trial ONLY after you have carefully read this information sheet and after you have had a THOROUGH DISCUSSION with a member of the study team, who will dedicate the NECESSARY TIME to ensure you fully understand what is being proposed.

A. PREMISE

Dear Madam/Sir,
We invite you to take part in the clinical trial described below.

You have the right to be informed about the purpose and characteristics of the trial so that you can decide freely and knowingly whether to participate.

This document aims to inform you about the nature of the trial, its purpose, what participation will involve for you, including your rights and responsibilities.

Please read carefully what follows. The researchers involved in this project, listed at the beginning of this document, are available to answer your questions. No question that comes to your mind is trivial—do not hesitate to ask!

The proposed study is aimed exclusively at collecting scientific data through observations and experimental assessments. The planned procedures do not include interventions with therapeutic or curative intent. Your participation will not directly affect the course of your disease nor the treatment you are receiving outside this trial.

In addition to speaking with us, you may discuss the proposal in this document with your family doctor, relatives, and other people you trust. Take all the time you need to decide. You may take home an unsigned copy of this document to think about it or discuss it with others before making a decision.

If you decide not to participate in the trial, you will still receive the best possible care for patients with your condition/disease.

Your refusal will not be interpreted in any way as a lack of trust.

IF APPLICABLE:
To facilitate understanding of this document, the trial center (OTHERS: SPECIFY) provides a cultural mediator able to convey the contents using methods and language most suitable for you.

IF APPLICABLE:
If you are not able to sign the informed consent, consent may be provided and recorded by appropriate alternative means, for example audio or video recordings, in the presence of at least one impartial witness.

Once you have read this form, received answers to any questions, and (if you decide) agreed to participate in the trial, you will be asked to sign a consent form, and you will receive a paper copy.

The Principal Investigator

B. INFORMATION SECTION

GENERAL SUMMARY OF THE TRIAL: KEY INFORMATION (no more than 1–2 pages)

This section aims to present a concise overview of the key aspects of the trial you are being invited to join. The following sections provide more details, to allow you to decide whether or not to give fully informed consent to participate.

• Why am I being asked to participate in this trial?

You are being asked to participate in this trial because we want to study how an upper-limb motor rehabilitation program may influence cognitive functions in patients with neurological and neurodegenerative conditions. Your participation will help us understand whether this type of treatment can improve not only movement ability but also important functions such as memory and attention. The results of this study may contribute to developing more effective rehabilitation approaches for people facing these challenges.

You were included among those invited to participate because you have certain clinical characteristics, which will be specified in Section C.

• What are the objectives of the trial? How many centers and patients will take part?

The main objectives of this trial are:

1. To evaluate the effects of an upper-limb motor rehabilitation program in patients with neurological and neurodegenerative conditions.
2. To analyze the impact of this program on cognitive functions, such as memory, attention, and problem-solving skills.
3. To identify possible correlations between improvements in motor and cognitive abilities.

The assessments and treatments planned in this trial do not have direct therapeutic purposes. The study is exclusively observational and experimental in nature. Therefore, participants should not expect immediate clinical improvements as a consequence of participation.

Approximately XX patients will be involved in this trial. This will allow us to collect meaningful data and have a broad basis for the analysis of results.

• Is deciding whether to participate my free choice?

You are free to choose whether or not to participate in the trial. Even after agreeing, you may change your mind at any time.

• If I decide not to consent to participation in the trial, what options do I have?

If you decide not to join the trial, you may still be followed by the clinical center providing your care, and you will be treated using the best approved (non-experimental) therapeutic methods for your disease.
In addition, you may participate in another trial that may be ongoing.

• What happens if I decide to participate in the trial?

[INDICATE THE PERIOD OF TIME DURING WHICH THE PATIENT WILL RECEIVE THE TREATMENT OR THE INTERVENTION OR WILL BE IN FOLLOW-UP.]

If you decide to participate in the trial, you will be assigned to one of two groups:

1. SBRR Group: You will receive a motor and cognitive rehabilitation program assisted by robotic and sensor-based devices, such as Motore, Armeo Senso, Hand Tutor, Armeo Power, Armeo Spring, Pablo, Amadeo, and Diego. This approach aims to improve motor and cognitive abilities through innovative technologies.
2. SCT Group: You will receive conventional motor rehabilitation. In this case as well, the program includes 60-minute sessions, 2–3 times per week, for a total of 25 sessions.

In both groups, cognitive and motor assessments will be carried out at the beginning and at the end of treatment, in order to monitor progress and the effectiveness of the program.

• What are the risks and benefits if I participate in the trial?

Participation in this trial may involve both risks and benefits. It is important to consider them carefully before making a decision.

Expected benefits
[DESCRIBE THE EXPECTED BENEFITS CLEARLY AND CONCISELY, REFERRING—DEPENDING ON THE TYPE OF STUDY—TO: (1) BENEFITS FOR THE PATIENT PARTICIPATING IN THE TRIAL; (2) BENEFITS FOR FUTURE PATIENTS AND FOR THE ACQUISITION OF GREATER KNOWLEDGE.]

Benefits for the patient:

- Access to innovative treatments: By participating, you will have the opportunity to receive a rehabilitation program that includes advanced technologies, potentially more effective than conventional methods.
- Careful monitoring: During treatment, you will receive regular assessments of your motor and cognitive abilities, allowing more accurate follow-up of your condition.

Benefits for other patients:

- Contribution to research: Your participation will help generate important data that may improve future rehabilitation practices for other people with similar conditions.

Potential risks
We want to ensure that you understand from the outset some possible risks: additional information can be found in the next section, "What risks might I face if I participate in this trial?"

[DESCRIBE THE RISKS IN GENERAL TERMS.]

- Physical discomfort: You may experience fatigue or discomfort during rehabilitation sessions, especially if the treatment involves intense physical activity.
- Emotional reactions: Undergoing rehabilitation may trigger emotions such as frustration or anxiety, especially if progress is slow.
- Treatment limitations: If you are assigned to the conventional rehabilitation group, you may not receive the same advanced technologies available in the SBRR group.

• Is consent final? Can I decide to withdraw from the clinical trial (voluntary withdrawal)?

You may decide to withdraw from the trial at any time and for any reason, without having to justify your decision.

If you decide not to participate anymore, please inform one of the study physicians as soon as possible: it is important to stop the treatment safely. The physician may consider a final follow-up visit/exam appropriate.

The physician will keep you informed of any changes in the trial that could influence your willingness to participate.

• Are there reasons why the trial might be stopped not at my request (early termination)?

Yes. The study physician may decide to stop your participation in the trial if:

- Your health conditions change and participating in the trial becomes potentially harmful;
- New information becomes available and the trial is no longer in your best interest;
- You do not follow the agreed rules for participation in the trial;
- For women: you become pregnant during the trial;
- The trial is interrupted by the competent authorities or by the sponsor.

[IN ANY CASE, SPECIFY THE NEED/OPPORTUNITY TO CONTINUE SCHEDULED FOLLOW-UP VISITS IN THE EVENT OF WITHDRAWAL OF CONSENT, SUSPENSION OF THE TRIAL, PREGNANCY, OR OTHER.]

C. INFORMATION SECTION. ADDITIONAL DETAILS

1. What is the purpose of the trial? (no more than ½ page)

[PROVIDE A CLEAR, CONCISE, AND PHASE-SPECIFIC EXPLANATION OF WHY THE RESEARCH IS BEING CONDUCTED.]

The purpose of this trial is to evaluate the effectiveness of a motor and cognitive rehabilitation program assisted by robotic and sensor-based devices for patients with neurological and neurodegenerative conditions. We want to explore how this innovative approach can improve upper-limb motor skills, enabling patients to perform daily activities more easily; evaluate the impact on cognition, analyzing whether and how motor improvements translate into benefits for cognitive functions such as memory, attention, and problem-solving skills; compare the effectiveness of robot-assisted treatment with conventional motor rehabilitation, to determine which method provides superior results for patient recovery; collect meaningful data that can contribute to research in the field of neurorehabilitation, informing future clinical practices and developing more personalized treatment protocols.

Through this study, we aim to improve patients' quality of life and provide concrete answers to a growing need in the management of neurological conditions.

2. What are the comparison patient groups? What is the intervention under investigation?

For this study, XX patients will be enrolled: XX with Parkinson's disease, XX with Multiple Sclerosis, and XX with stroke, divided into 2 groups (a group receiving robotic rehabilitation and a group receiving conventional rehabilitation).

Inclusion criteria
• Age 18–75 years;
• FMA-UL 0–31: eligible for exoskeletons and robotic devices with high support (Armeo Power, Amadeo, Motore);
• FMA-UL 32–47: eligible for end-effectors with medium support (Armeo Spring, Hand Tutor, Diego);
• FMA-UL 48–52: eligible for sensor-based devices with low support (Pablo, Diego, Armeo Senso);
• MoCA: ≤ 20.

Exclusion criteria
• Severe cognitive disorders;
• Behavioral disorders;
• Sensory disorders.

During the rehabilitation training session, the patient will use advanced robotic devices designed to support upper-limb movement. Each session will last 60 minutes and will include a series of targeted exercises, personalized according to the patient's individual needs. The exercises will include:
• Grasp-and-release movements: using devices such as Hand Tutor or Armeo Spring, the patient will perform grasp exercises to improve strength and coordination;
• Pulling and pushing exercises: using Armeo Senso or Pablo, the patient will be encouraged to perform pulling and pushing movements, promoting upper-limb mobility and improving motor integration;
• Coordination activities: patients will use systems such as Diego to perform exercises that stimulate hand–eye coordination and dexterity, useful for daily activities.

Each session will be monitored by a rehabilitation professional who will provide feedback and support to ensure exercises are performed correctly and safely. The goal is to promote progressive and functional recovery by adapting exercises to the patient's abilities to maximize rehabilitation benefits.

• A rehabilitation training session using advanced upper-limb technologies consists of: _____. If you have completed the trial and benefited from the new treatment, you will have the possibility to participate in repeated rehabilitation sessions.
• You may be randomly assigned to the experimental or control group. If you are in the experimental group, you will undergo rehabilitation training using advanced technologies for upper-limb rehabilitation. If you are assigned to the control group, you will undergo conventional upper-limb rehabilitation training.

3. What tests and procedures are planned if I participate in the trial? (section no longer than ¾ page, unless many exams/procedures are planned)

Each participant will undergo a neuropsychological assessment before (T0) and after treatment (T1), conducted by a neuropsychologist to ensure objectivity. The tests will evaluate the following cognitive domains:
• Parkinson's disease population: attention, memory, executive functions, language, and visuospatial abilities.

• Multiple Sclerosis population: memory, attention, and executive functions.
• Post-stroke population: attention, memory, executive functions, and visuospatial abilities.

At the end of training, we will use scales to evaluate device usability and the achievement of individual goals.

In addition, each participant will undergo a motor assessment (T0 and T1) conducted by a physiotherapist, who will analyze motor function, coordination, and sensation.

4. What risks might I face if I participate in the trial? (section no longer than 4 pages)

Although rare, undesirable reactions to the devices used or to the proposed exercises may occur.

5. What will my commitment be and what responsibilities will I have if I decide to participate? (section no longer than ½ page)

PARTICIPATION IN THIS STUDY INCLUDES 25 REHABILITATION TRAINING SESSIONS, 2–3 TIMES PER WEEK, LASTING APPROXIMATELY 60 MINUTES PER SESSION.

[PROVIDE INFORMATION ABOUT PARTICIPANT RESPONSIBILITIES, IN PARTICULAR:]
• Carefully follow the indications and requests of the healthcare staff involved in the trial and ensure attendance at appointments.
• Inform the trial physician:
o of all medicines you are taking, including non-conventional medicine products;
o of any side effects that occur during the trial;
o of any visit or hospitalization in facilities other than the study center;
o of current or previous participation in other clinical trials.

6. Will I have to bear costs to participate in the trial? Will I be reimbursed for any expenses? Will I receive compensation?

[CLARIFY THAT PARTICIPATION IN THE TRIAL DOES NOT INVOLVE COSTS AND THE PERSON WILL NOT BE COMPENSATED IN ANY WAY (THE LAW EXPRESSLY FORBIDS IT); IF TRAVEL/ACCOMMODATION REIMBURSEMENTS EXIST, THE MODALITIES MUST BE SPECIFIED.]

No costs related to participation in the trial are expected to be borne by you, as these are fully covered by the study center (or by the sponsor, if present).
No financial compensation is provided for participation in the trial.

7. What happens if I suffer harm as a consequence of participation in the trial?

Participation in a clinical trial may involve inconveniences and risks that cannot be determined in advance. For this reason, the clinical trial provides insurance coverage to protect your participation.

In compliance with current laws, insurance is in place to cover any damage suffered due to participation in the trial for the entire duration of the trial, covering the civil liability of the investigator and the sponsor.

It should be specified that, according to the Ministerial Decree of 14 July 2009, the insurance policy does not cover amounts exceeding the maximum coverage limit and is valid only for damages for which a claim for compensation is submitted no later than the period provided in the policy

([INDICATE THE NUMBER OF MONTHS]). This limitation does not affect your right to obtain compensation from the party responsible for any damage (for the protection of the trial participant).

8. How will my health data, including identifying data, be processed during the trial, and who will have access to it?

Your data—especially personal and health data, and only to the extent indispensable to the purpose of the trial and for pharmacovigilance—will be processed in compliance with EU Regulation 2016/679 (GDPR, General Data Protection Regulation) and Legislative Decree 10 August 2018, no. 101. In practical terms, the documents related to the participant will be stored in a secure place and will not report your name in full; instead, an identification code known only to the researchers will be used.

The data, once anonymized, may be subject to inspection by regulatory bodies and used for scientific publications (journals, conferences).

Your clinical data collected for the purposes of the trial, as well as the results of examinations performed, will be kept for the time required by regulations and subsequently destroyed. They will not be destroyed only if: (a) it is no longer possible to trace them back to your identity because they have been anonymized during the trial; (b) you have provided specific informed consent.

If personal data are transferred to a third country or an international organization, all safeguards provided for by Article 46 of the GDPR 679/2016 regarding the transfer will be adopted.

Further information is included in the attached authorization form for personal data processing.

9. How will my biological samples collected for the purposes of the trial be processed, and who will have access to them?

Once the trial is finished, your samples will be destroyed. They will not be destroyed only if: (a) it is no longer possible to trace them back to your identity because they have been anonymized during the trial itself; or (b) you have provided specific informed consent and there is an agreement with the biobank for sample storage.

10. How can I access the results of the trial?

Once the trial has been completed and all resulting data have been collected, the data will be analyzed to draw conclusions. The investigators and the sponsor undertake to make them available to the scientific community.

Regulations provide the possibility for participants to access the results of the trial. Therefore, you may ask the study physician to communicate the overall results of the trial to you.

11. Has the trial been approved by the Ethics Committee?

The trial protocol proposed to you has been reviewed and approved by the Local Ethics Committee of IRCCS Centro Neurolesi Bonino Pulejo. The Ethics Committee verified compliance of the trial with Good Clinical Practice standards and the ethical principles expressed in the Declaration of Helsinki, and that your safety, rights, and well-being are protected.

12. Who can I contact to obtain more information about the clinical trial I am invited to participate in?

[PROVIDE THE NAMES AND CONTACT DETAILS OF THE PEOPLE WHOM THE PERSON CAN CONTACT FOR FURTHER INFORMATION.]

Dr. Desirèe Latella (desiree.latella@irccsme.it) – Dr. Rocco Salvatore Calabrò (roccos.calabro@irccsme.it)

13. If I join the trial, whom can I contact in case of need?

For any questions or unforeseen or unplanned event during the trial (questions related to ongoing treatment, side effects, decision to withdraw from the trial, etc.), you may contact:

[PROVIDE NAMES AND CONTACT DETAILS OF THE STUDY CENTER STAFF THE PARTICIPANT MAY CONTACT (Doctor [Desirèe Latella], telephone no. 090 60128179, e-mail desiree.latella@irccsme.it).]

_____ //_____ _____ _____

Printed full name of the physician Date Time Signature
who delivered the information sheet

Attachments
• Insurance policy
• Consent form for personal data processing

D. CONSENT EXPRESSION SECTION

(Note: 1 copy for the participant, 1 copy for the trial lead)

Trial title: Exploring cognitive recovery: the impact of sensor-based upper-limb robotic rehabilitation in neurological and neurodegenerative disorders
Protocol code, version, and date: CROSS-ND Version 01 of 05/11/2024
Sponsor/Funder: IRCCS Centro Neurolesi Bonino Pulejo
Principal Investigator: DESIRÈE LATELLA – IRCCS Centro Neurolesi Bonino Pulejo

I, the undersigned _____
born in _____ on //_____

I DECLARE

☐ that I have received from Dr. _____ comprehensive explanations regarding the request to participate in the above research, as reported in the information section forming part of this consent, of which I was given a copy on _____ at _____ (indicate date and time of delivery);

☐ that the nature, objectives, procedures, expected benefits, possible risks and inconveniences, and alternative treatment options compared with the proposed clinical trial have been clearly explained to me and that I have understood them;

☐ that I have had the opportunity to ask any questions to the study investigator and that I have received satisfactory answers;

☐ that I have had sufficient time to reflect on the information received;

☐ that I have had sufficient time to discuss it with third parties;

☐ that I have been informed that the trial protocol and all forms used have received a favorable opinion from the competent Ethics Committee;

☐ that I am aware that the research may be interrupted at any time by decision of the person responsible for the research;

☐ that I have been informed that I will be made aware of any new data that could compromise the safety of the research and that, for any problem or further questions, I may contact the physicians caring for me;

☐ that, for the best protection of my health, I am aware of the importance (and my responsibility) to inform my general practitioner about the trial I agree to participate in. I am aware of the importance of providing all information concerning me (medications, side effects, etc.) to the investigator;

☐ that I have been informed that the results will be made known to the scientific community, safeguarding my identity according to current privacy regulations;

☐ that I am aware that any choice expressed in this consent form may be revoked at any time and without any justification;

☐ that I have received a copy of this consent form.

I THEREFORE DECLARE THAT I

☐ wish to participate in the trial

☐ wish ☐ do NOT wish to be informed of all unexpected findings regarding my present or future health that may incidentally emerge from the investigations planned in the trial, including genetic findings, when this may involve possible benefits

☐ wish ☐ do NOT wish to be informed of unexpected findings regarding my present or future health only when this may be useful for my healthcare or to enable me to make informed reproductive choices

☐ wish ☐ do NOT wish to be contacted again after the end of the trial to provide information about my health status (this applies only to contacts not provided as follow-up by the study protocol)

If applicable:
☐ accept ☐ do NOT accept the use of contraceptive drugs

_____ //_____ _____ _____
Printed full name of adult patient Date Time Signature

_____ //_____ _____ _____
Printed full name of legal representative Date Time Signature

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STATEMENT OF THE PHYSICIAN WHO OBTAINED CONSENT

(Patient's name, place and date of birth)

Trial title: Exploring cognitive recovery: the impact of sensor-based motor rehabilitation in neurological and neurodegenerative disorders
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Sponsor: IRCCS Centro Neurolesi Bonino Pulejo
Principal Investigator: DESIRÈE LATELLA – IRCCS Centro Neurolesi Bonino Pulejo

I, the undersigned Prof./Dr. _____, in my role as Principal Investigator (or delegate of the Principal Investigator)

Surname _____ Name _____

DECLARE
that the patient has voluntarily consented to participate in the trial.

I also DECLARE that I have:
☐ provided the patient with comprehensive explanations regarding the aims of the trial, procedures, possible risks and benefits, and possible alternatives;
☐ verified that the patient has sufficiently understood the information provided;
☐ given the patient the necessary time and the possibility to ask questions about the trial;
☐ clearly explained the possibility to withdraw from the trial at any time or to change the choices made;
☐ not exercised any coercion or undue influence in requesting this consent;
☐ provided the patient with information on how the trial results will be communicated to them.

Place and date Time